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Application of Headspace-SIFT-MS to Direct Analysis of Hazardous Volatiles in Drinking Water

Mark J. Perkins [1] and Vaughan S. Langford [2,*]

[1] Element Materials Technology Laboratory Instrumentation, Wellbrook Court, Girton Rd., Girton, Cambridge CB3 0NA, UK
[2] Syft Technologies Limited, 68 Saint Asaph Street, Christchurch Central City, Christchurch 8011, New Zealand
* Correspondence: vaughan.langford@syft.com

Abstract: Harmful volatile organic compounds (VOCs) are present in drinking water due to anthropogenic activities, such as oil refining (e.g., benzene) and disinfection (e.g., the so-called trihalomethanes, THMs). Gas chromatography (GC)-based techniques are widely applied for analysis of these compounds in the laboratory but have some throughput drawbacks due to sample preparation and the extended analysis time (due to chromatographic separation). Selected ion flow tube mass spectrometry (SIFT-MS) is a direct-injection mass spectrometry (DIMS) technique that has potential to reduce sample preparation and analysis times through direct analysis of aqueous headspace with no preconcentration, drying, or other water management. This study applies headspace-SIFT-MS to the analysis of benzene, related petroleum aromatics, and THMs to evaluate the potential for enhanced sample throughput for drinking water analysis (10 samples per hour). Headspace-SIFT-MS achieved a limit of quantitation (LOQ) of 0.1 to 0.2 μg L^{-1} for benzene, toluene, ethylbenzene and xylenes (BTEX), and 1 to 2 μg L^{-1} for the THMs. These LOQs achieve the current European Union and United States regulatory limits but are higher than modern GC methods. Therefore, the potential application of SIFT-MS is envisaged to lie in rapid screening in the laboratory, or field-based real-time monitoring.

Keywords: SIFT-MS; volatile organic compound (VOC); BTEX; THM; headspace; instrumental analysis; direct-injection mass spectrometry (DIMS); disinfection byproduct

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1. Introduction

Local authorities are typically responsible for maintaining their drinking water supplies at standards specified by the relevant national regulatory authority (e.g., the United States Environmental Protection Agency (US EPA) [1] or broader regional agency, as in the case of the European Union's member states [2]. Broadly, these regulations set maximum contaminant levels (MCLs) for microorganisms, disinfectants, disinfection byproducts, inorganic chemicals, organic chemicals (both volatile and semivolatile), and radionuclides [3]. Among the wide range of volatile organic compounds (VOCs) that can potentially pollute drinking water [4], the low-molecular-weight aromatic hydrocarbons (benzene, toluene, ethylbenzene, and the xylenes; BTEX) and the trihalomethanes (THMs; chloroform, bromodichloromethane, dibromochloromethane, and bromoform) furnish useful test sets for evaluating the performance of new analytical approaches. This is particularly true for benzene and the THMs which have lower MCLs because of their higher toxicities. Benzene typically arises from factory discharges and leaching from gas storage tanks and landfills fossil fuels [4], whereas THMs are a byproduct of chlorinated disinfection agents used to inactivate pathogenic organisms in drinking water [1].

Conventional analysis of BTEX and THMs is laboratory-based and utilizes gas chromatography (GC) for the separation of analytes and various detectors for quantitation. Purge-and-trap (PT) sample preparation coupled with GC/mass spectrometry (GC/MS) is required by the US EPA [1] using either method 524.3 [5] or 524.4 [6]. One of the challenges for conventional GC/MS methods is how to practically address sample throughput limitations because the chromatographic separation step is the limiting factor [7]. Direct-injection mass spectrometry (DIMS) techniques have the potential to increase sample throughput through (1) elimination of the chromatographic separation and (2) application of soft chemical ionization coupled with mass spectrometric detection [7]. Potentially suitable commercially available DIMS techniques for VOC analysis are atmospheric pressure chemical ionization-MS (APCI-MS), proton transfer reaction mass spectrometry (PTR-MS) and selected ion flow tube mass spectrometry (SIFT-MS) [8,9], although to date only SIFT-MS has been applied to routine analysis to the best of our knowledge [7]. PTR-MS has been applied to inline water analysis, but as these involve either a membrane interface [10], or formation of a continuous spray (e.g., [11,12]) from which to extract the sample for analysis, those studies are of less relevance here, but do point toward potential continuous monitoring applications.

This study benchmarks headspace-SIFT-MS against performance criteria given in the regulatory PT-GC/MS methods [5,6] and a recent study utilizing a static headspace-GC/MS analytical approach (for disinfection byproducts, DBPs) [13]. Previous work has demonstrated that headspace-SIFT-MS provides higher sample throughputs than headspace-GC/MS methods [14,15]. However, the few reported measurements on aqueous headspace [16–18] have not generally achieved the required MCLs or maximum contaminant level goals (MCLGs; [1,4] for benzene and the individual THMs (or compounds with similar properties in those limited studies). The purpose of this study was to develop an analytical methodology that could achieve, where possible, the required MCLs, and hence evaluate the potential of headspace-SIFT-MS for routine and real-time BTEX and THM analysis in drinking water.

2. Materials and Methods

2.1. Target Compounds, Working Solutions, and Test Samples

Suppliers and purities of the eight target compounds (benzene, toluene, ethylbenzene, *m*-xylene (representing the sum of xylene isomers measurable using SIFT-MS), chloroform, bromodichloromethane, dibromochloromethane, and bromoform) are given in Table 1; all were utilized without further purification. Dimethyl sulfoxide (DMSO; Sigma Aldrich, ≥99.5%) was used as the solvent in which stock solutions were prepared [18]. All headspace standard solutions were prepared using a 10% NaCl solution (18 MΩ Milli-Q water).

Table 1. Target compounds in this study, limits in drinking water for the EU [2] and maximum contaminant level (MCL) for the United States [1] and the State of Florida [19], supplier, and purity. Limits are μg L^{-1} in solution.

Name	CAS No.	EU Limit [2]	US Limit [1]	Florida Limit [19]	Supplier	Purity
Benzene	71-43-2	1	5	2	Fluka (St. Louis, MO, USA)	>99.9%
Ethylbenzene	100-41-4	N/A	700	80	Sigma Aldrich (St. Louis, MO, USA)	99.8%
Toluene	108-88-3	N/A	1000	56	Aldrich	99%
Xylene (sum of isomers; *m*-used *)	108-38-3	N/A	10,000	N/A	Sigma Aldrich	>99%
Bromodichloromethane	75-27-4	**	0 ***	2.1	Sigma Aldrich	≥97%
Bromoform	75-25-2	**	0 ***	15	Sigma Aldrich	99%
Chloroform	67-66-3	**	70 ***	60	Sigma Aldrich	>99%
Dibromochloromethane	124-48-1	**	60 ***	1.8	Sigma Aldrich	98%

* SIFT-MS cannot distinguish the xylene isomers, so a total is measured. Hence, just the *m*-xylene isomer was used in this study. ** The EU regulation [2] specifies only a total THM concentration of 100 μg L^{-1}. *** Individual THMs are maximum contaminant level goals (MCLG) for USA. The total THM concentration (MCL) is 80 μg L^{-1} [1,4].

The THM and BTEX compounds were prepared as a single primary stock solution containing 50 μg mL^{-1} of individual THMs and 5 μg mL^{-1} of individual BTEX compounds in DMSO. From this an intermediate stock solution was prepared by adding 100 μL of primary stock to 10 mL of MilliQ water. A final working stock solution was prepared from the intermediate stock by adding 30 µL of stock solution to 15 mL of MilliQ water. All subsequent analytical standards were prepared from the final working stock solution. Additionally, a final working stock solution was prepared containing just chloroform, by following an identical procedure to that described above.

Calibration standards were prepared at 50 µg L^{-1} and 5 µg L^{-1}, for the THMs and BTEX compounds, respectively, by suitable dilution of the working stock solution in 10 mL of 10% NaCl solution. Additionally, 50 µg L^{-1} chloroform standards were prepared by suitable dilution of the chloroform working stock solution in 10 mL of 10% NaCl.

Although the focus of this article is primarily on analytical performance, practical application to real samples must be considered. Drinking water from the town supply in Girton in Cambridgeshire, UK, was utilized. Girton drinking water is sourced from ground water reservoirs, then sieved, chemically treated to remove fine particles and bacteria, filtered using gravel and carbon, and finally disinfected using chlorine prior to distribution to residential and commercial properties. Samples used were collected and analyzed on 17 August 2022.

2.2. Instrumentation

The SIFT-MS technique has been described in detail elsewhere [20,21]. Briefly, SIFT-MS is a DIMS technique that can analyze air and headspace continuously by using a soft chemical ionization approach that efficiently ionizes a very broad range of VOCs, but does not ionize the bulk constituents of air (e.g., N_2, O_2, Ar, and water). A microwave discharge in air is used to generate the reagent (or precursor) ions, with eight available (H_3O^+, NO^+, $O_2^{+\bullet}$, $O^{-\bullet}$, OH^-, $O_2^{-\bullet}$, NO_2^- and NO_3^-) on the SIFT-MS instrument used in this study (Voice200*ultra*; Syft Technologies Limited, Christchurch, New Zealand) [22]. Instrument detection limits in the part-per-trillion by volume (pptV) range are typically achieved for 1-s ion dwell times for direct analysis of air with no preconcentration or drying required [23,24].

Headspace analysis was conducted using a SIFT-MS instrument (operating on helium carrier gas) integrated with a syringe-injection autosampler (Multi-Purpose Sampler (MPS) Robotic Pro: GERSTEL, Mülheim, Germany) [15]. The autosampler was controlled using Maestro software (GERSTEL), which also includes efficient task sequencing. In this study, each sample was incubated in one of two six-position agitators (GERSTEL) on the autosampler rail, enabling them to form—via software—a virtual 12-position agitator/incubator. Headspace analysis was carried out from 20-mL sample vials located on standard headspace vial racks (GERSTEL).

Note that the units presented in this article for headspace concentration determinations are shown as parts-per-billion by volume (ppbV). These are the "natural" units for quantification in direct gas phase analysis using SIFT-MS [20], but in the context of headspace analysis they represent a convenient normalized response factor from which concentrations in solution (at parts-per-billion mass:volume) can be derived via a calibration curve [18]. The instrument software calculates concentrations for each quantitation ion individually. In routine operation, if two or more quantitation ions are utilized for a given compound, then the software cross-compares these measurements and rejects from the averaging process (as "probably interfered with") those concentrations that lie above the lowest measurement by a user-chosen percentage (typically > 20%). This approach is modified for the THMs, as described in Section 2.3.1.

2.3. Method Development

2.3.1. SIFT-MS Method

Relatively low ion count levels in SIFT-MS instruments (compared to GC/MS) necessitate relatively long dwell times for the former to achieve good data averaging. This means that measurement precision and hence limits of detection and quantitation (LODs and LOQs) [25] are significantly improved for targeted analysis in selected ion mode (SIM;

also called multiple ion monitoring, MIM). Initial method development evaluated a wider range of ions for each compound than were utilized in this study. The most sensitive and selective quantitation ions were identified, which enable better LOQs to be achieved, and these are summarized in Table 2 (i.e., unused product ions are not shown).

Table 2. Reagent ion-product ion pairs (product ions identified by mass-to charge ratios) used to quantify target compounds, with branching ratio (as a percentage). For simplicity, other unused ion products of each compound are not shown. See the text for resolution of bromodichloromethane from chloroform, and ethylbenzene from the sum of xylene isomers.

Compound, Molecular Formula	**Reagent Ion**	**Product Ion Formula**	**Product Ion *m*/*z***	**Ion Signal Ratios**	**Reference**
Benzene, C_6H_6	NO^+	$C_6H_6^+$	78	76%	[26]
Bromodichloromethane, $CHBrCl_2$	$O_2^{+\bullet}$	$CH^{35}Cl_2^+$	83	56%	This work
	$O_2^{+\bullet}$	$CH^{35}Cl^{37}Cl^+$	85	38%	This work
Bromoform, $CHBr_3$	$O_2^{+\bullet}$	$CH^{79}Br_2^+$	171	25%	[27]
	$O_2^{+\bullet}$	$CH^{79}Br^{81}Br^+$	173	50%	[27]
	$O_2^{+\bullet}$	$CH^{81}Br_2^+$	175	25%	[27]
Chloroform, $CHCl_3$	$O_2^{+\bullet}$	$CH^{35}Cl_2^+$	83	56%	[28]
	$O_2^{+\bullet}$	$CH^{35}Cl^{37}Cl^+$	85	38%	[28]
	OH^-	$C^{35}Cl_3^+$	−117	42%	[29]
	OH^-	$C^{35}Cl_2{}^{37}Cl^+$	−119	42%	[29]
Dibromochloromethane, $CHBr_2Cl$	$O_2^{+\bullet}$	$CH^{79}Br\ {}^{35}Cl^+$	127	38%	This work
	$O_2^{+\bullet}$	$CH^{35}Cl^{37}Cl^+$	129	50%	This work
Ethylbenzene, C_8H_{10}	NO^+	$C_8H_{10}^+$	106	100%	[26]
	$O_2^{+\bullet}$	$C_7H_7^+$	91	70%	[26]
	$O_2^{+\bullet}$	$C_8H_{10}^+$	106	30%	[26]
Toluene, C_7H_7	NO^+	$C_7H_8^+$	92	100%	[26]
Xylene (all isomers; *m*-used), C_8H_{10}	NO^+	$C_8H_{10}^+$	106	100%	[26]
	$O_2^{+\bullet}$	$C_7H_7^+$	91	20%	[26]
	$O_2^{+\bullet}$	$C_8H_{10}^+$	106	80%	[26]

It is evident from Table 2 that use of positive ion mode alone is inadequate for this target compound list because bromodichloromethane and chloroform cannot be distinguished; of the positively charged reagent ions, only $O_2^{+\bullet}$ reacts with them rapidly (i.e., with high sensitivity) and it produces $CHCl_2^+$ through loss of $Br^\bullet$ and $Cl^\bullet$, respectively. By utilizing OH^-, however, chloroform was analyzed independently of bromodichloromethane, and this measurement was subtracted from the total obtained using $O_2^{+\bullet}$. (Note that bromodichloromethane reactions with OH^- are described in the literature [30], but analytical sensitivity with OH^- was considerably reduced compared to chloroform. Hence, chloroform was selected for independent quantification and used for subtraction.) To achieve positive and negative ionization efficiently, the dual sampling approach described in Ref. [18] was utilized, enabling the unique polarity-switching feature of SIFT-MS to be leveraged within a single analysis on a single vial (Figure 1). As chloroform and bromodichloromethane have different reaction rates with $O_2^{+\bullet}$ (evident in different concentration measurements using the same reagent-product ion pairs in Figure 1) it is necessary to obtain a relative response factor for chloroform/bromodichloromethane. This factor can then be applied when the chloroform concentration is subtracted from the combined $O_2^{+\bullet}$

response. The single-component chloroform standard from the calibration (injection on the right-hand side of Figure 1) is used to calculate the response factor.

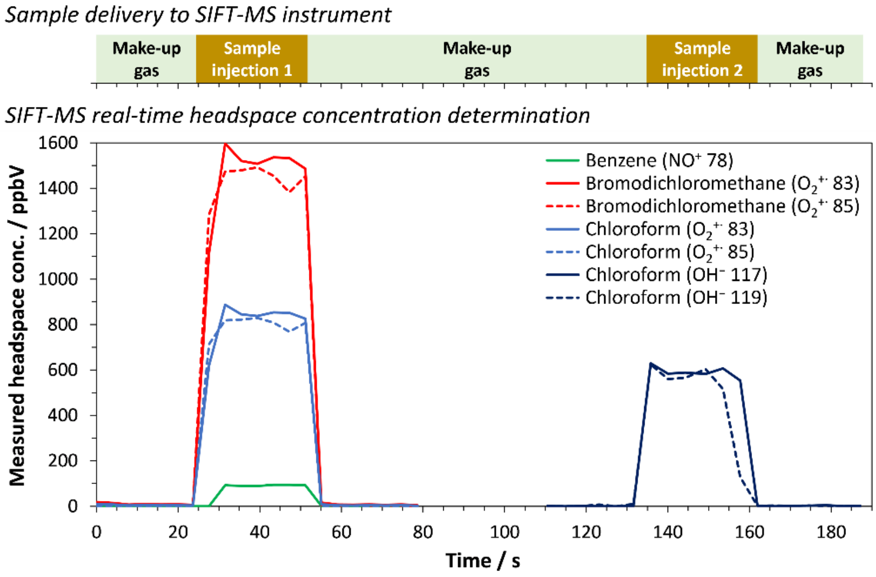


Figure 1. Injections for dual sampling of a single vial (calibration levels of 5 and 50 µg L^{-1}, for BTEX and the THMs, respectively), enabling SIFT-MS analysis using both positive (left-hand injection) and negative (right-hand) reagent ions in a single run. Each trace represents real-time measurement of a given quantitation ion, with benzene, bromodichloromethane, and chloroform product ions used as examples.

A second speciation challenge is posed by separation of ethylbenzene from the xylene isomers. As shown in Ref. [26], all positively charged SIFT-MS reagent ions yield the same fragment ions, though for $O_2^{+\bullet}$ the relative proportions of the charge transfer product (*m/z* 106) and the product losing $CH_3^{\bullet}$ (*m/z* 91) essentially swap between ethylbenzene and the xylenes. This enables a calibration approach to be utilized to separate them [16] if the matrix itself does not contribute interfering ions for $O_2^{+\bullet}$ *m/z* 91 and/or 106. A calibration curve containing varying concentrations of xylene and ethylbenzene was prepared and the relative responses to the *m/z* 91 and 106 product ions (Table 2) were used to extract the ethylbenzene and xylene contributions. As branching ratios for SIFT-MS are highly stable, this curve can be generated prior to any routine analyses being conducted and used from that time forward. Note, however, that the xylene isomers cannot be separated using the current SIFT-MS reagent ions; hence, a total xylene concentration is reported.

Quantitation was conducted using a calibration approach that is closely aligned with routine analysis procedures applied to chromatographic techniques since it is both simple and rapid for automated SIFT-MS instruments [7]. This is a relatively recent innovation for SIFT-MS because there is substantial extant literature that demonstrates SIFT-MS providing accurate absolute quantitation from first principles [20,31]. Although—when Henry's Law constants are known—solution concentrations can also be determined from first principles [32], routine calibration is better accepted within a routine analysis workflow. One practical benefit arises from quantifying using calibration: where library data are not available for a compound's reaction with a given reagent ion or need to be updated due to changed ionization conditions, the calibration approach bypasses the need to determine the reaction rate coefficients that are essential for absolute quantitation, the determination of which is a non-trivial procedure [20]. This approach was used to acquire the positive ion data for bromodichloromethane and dibromochloromethane (Table 2), which are not available in the literature to the best of our knowledge.

Calibrated concentrations were calculated for individual quantitation ions. For benzene and toluene, this is a trivial procedure as only one ion was used for these analytes. For ethylbenzene and xylene, a total concentration is reported using the NO^+ 106 product ion, while speciation proceeded as described above. For the THMs, the mean of the quantitation ions was reported as the final concentration (each of the ions in Table 2 is an isotopic variant of the same molecular ion). This approach diverges from the standard approach (Section 2.2) because averaging all ions improves the signal-to-noise ratio (SNR) and hence the limit of quantitation. It was justified for this matrix because there was good agreement between the isotopic ions in the test samples, suggesting an absence of interference of the ions. It should be noted, however, that this approach is not always viable due to more complex matrices (e.g., [33]) and the standard interference rejection approach performs better, albeit with potential reduction in SNR. The Supplementary Materials provide data by quantitation ion.

Blanks (10 mL of 18 MΩ Milli-Q water) were analyzed after every cross-check standard to ensure that carryover from high-level samples was minimized (no carryover was observed). Measured blank concentrations were subtracted from the standards and test samples.

2.3.2. Headspace Analysis Optimization

Optimization of parameters for generic aqueous headspace analysis using automated SIFT-MS was described in Ref. [18]. In this work, the goal was enhanced sensitivity. To this end, both the incubation temperature and the injection speed were increased (Table 3). As noted in the preceding section, the SIFT-MS method was optimized for sensitivity by selecting the minimum number of quantitation ions that provides the highest SNR for each analyte.

Table 3. Optimized parameters for enhanced sensitivity in headspace-SIFT-MS analysis of water compared with those for generic analysis of the same matrix [18] *.

Parameter	General-Purpose Aqueous Headspace Analysis [18]	High-Sensitivity Aqueous Headspace Analysis (This Study)
SIFT-MS sample analysis time	240 s	190 s
SIFT-MS product ion dwell time	200 ms	200 ms
Incubation time	20 min	20 min
Incubation temperature	60 °C	75 °C
Vial size	20 mL	20 mL
Volume of aqueous used	10 mL	10 mL
Headspace syringe volume	2.5 mL (2 injections) **	2.5 mL (2 injections) **
Syringe temperature	150 °C	150 °C
Headspace injection rate	50 $\mu L\ s^{-1}$	100 $\mu L\ s^{-1}$
Add NaCl	10% (1 g in 10 mL)	10% (1 g in 10 mL)
Quality control	Single point analysis, with cross-checks as required (6 repl. calibration standards at 1 ppm solution)	Single point analysis, with cross-checks as required (3 repl. calibration standards at 5 or 50 $\mu g\ L^{-1}$ for BTEX or THMs, respectively

* Both methods were developed using both positively and negatively charged reagent ions. ** Two consecutive 2.5 mL syringe headspace injections enable switching from $NO^+/O_2^{+\bullet}$ to OH^-.

3. Results

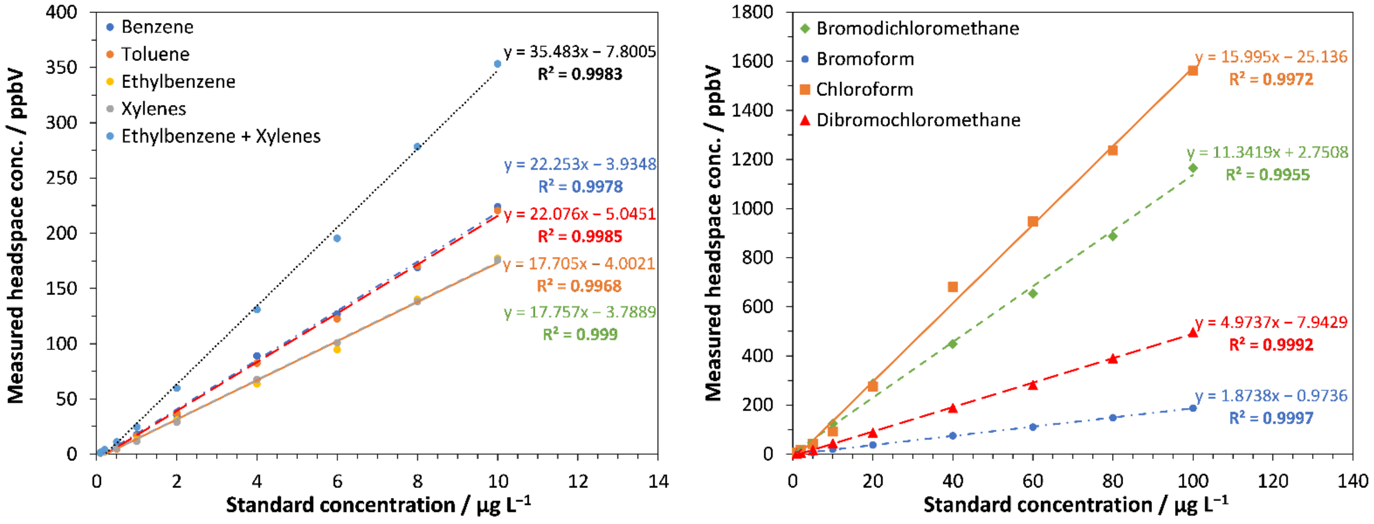
This section presents the results obtained using the optimized HS-SIFT-MS approach described in the previous section. The results are presented in terms of a limited method validation study since the previous work [18] enables judgments to be made on the likelihood of success of full method validation.

3.1. Specificity

The within-method specificity challenges (chloroform interference with bromodichloromethane and the similar ethylbenzene and xylene ion chemistries) were described in Section 2.3.1. In high-purity water, these issues are effectively addressed, and all components are resolved. However, as shown below, for several THMs there may be unidentified interference in drinking water measurements. Based on the SIFT-MS results alone, the agreement of the individual quantitation ions for a given compound suggest that several analytes are present above the LOQ because they match the halogen isotopic abundances expected from the target ions. However, to determine this conclusively a more substantial laboratory study utilizing GC/MS is required, which is beyond the scope of this work.

3.2. Linearity

Linearity was assessed over the range 0.1–10 and 1−100 µg L^{-1} for BTEX and the THMs, respectively. Figure 2 shows the results obtained for BTEX and the THMs, where for the latter the concentrations are calculated as a mean of the measurements calculated using the different quantitation ions (isotopic variants). For ethylbenzene and the xylenes, in addition to the speciated curves, the total ethylbenzene plus xylene concentration obtained using NO^+ is shown for reference, since in more complex matrices deconvolution is unsuccessful (see, for example, a recent study of wastewater treatment plant odor [33]). The Supplementary Materials tabulate the data for individual target ions and show linearity for the individual compounds (Tables S1 and S2 and Figures S1 and S2 for BTEX and the THMs, respectively). Linearity is very good, with linear regression coefficients (R^2) greater than 0.993 across all quantitation ions.



(**a**) (**b**)

Figure 2. Linearity of headspace measurements versus standard concentration averaged across product ions for each compound, showing the linear fit and its regression coefficient, R^2. (**a**) BTEX; (**b**) THMs.

3.3. Limit of Quantitation (LOQ) and Range

In SIFT-MS there is no baseline noise from which to calculate signal-to-noise ratios (S/N). Following [18], the approach taken was to determine the lower limit of quantitation (LLOQ) empirically based on the relative standard deviations (RSDs) of less than 20% across all related components. From method development, the LLOQ was estimated as lying within the 0.1−0.5 and 1−5 µg L^{-1} ranges in solution for BTEX and the THMs, respectively. Triplicate measurements were made at three concentrations across these ranges. Tables 4 and 5 summarize the results obtained for the BTEX and THM compounds, respectively, while Tables S3 and S4 of the Supplementary Materials provide data for all quantitation ions. For the two groups of compounds, the LLOQ lies on the lowest or middle standard, depending on the analyte, i.e., 0.1 or 0.2 µg L^{-1} for BTEX and 1 or 2 µg L^{-1} for the THMs. Interestingly, bromodichloromethane behaves similarly to the other THMs, even though it must be determined by subtraction of chloroform, as described in Section 2.3.1.

Table 4. Determination of the method LOQ for BTEX using solution concentrations of 0.1, 0.2, and 0.5 µg L^{-1}. Headspace concentrations, means and standard deviations (SD) are reported in ppbV and the RSD is reported as a percentage.

Solution Conc./µg L^{-1}	Replicate No./*Statistical Parameter*	Benzene	Toluene	Ethylbenzene *	Xylenes *
0.1	1	0.810	0.990	0.720	0.730
	2	0.880	0.530	0.727	0.595
	3	1.08	0.820	0.570	0.530
	Mean	0.923	0.780	0.672	0.619
	SD	0.114	0.190	0.073	0.083
	%RSD	12.4	24.3	10.8	13.5
0.2	1	3.31	2.26	2.04	1.46
	2	3.40	1.98	2.39	1.45
	3	2.79	2.08	2.24	1.59
	Mean	3.17	2.11	2.22	1.50
	SD	0.269	0.116	0.146	0.062
	%RSD	8.5	5.5	6.6	4.2
0.5	1	4.53	4.63	2.71	3.32
	2	3.94	3.89	3.34	3.45
	3	4.29	4.07	2.81	3.01
	Mean	4.25	4.20	2.95	3.26
	SD	0.242	0.315	0.277	0.186
	%RSD	5.7	7.5	9.4	5.7

* See Section 2.3.1 for deconvolution of ethylbenzene and the xylenes using the $O_2^{+\bullet}$ product ions.

Table 5. Determination of the method LOQ for the THMs using solution concentrations of 1, 2, and 5 µg L^{-1}. Headspace concentrations (in ppbV) are averaged across both/all quantitation ions used to target the compound. The RSD is reported as a percentage.

Solution Conc./µg L^{-1}	Replicate No./*Statistical Parameter*	Bromodichloromethane *	Bromoform	Chloroform	Dibromochloromethane
1	1	24.3	0.207	7.12	2.35
	2	33.4	2.02	6.77	2.20
	3	31.6	0.877	7.27	1.38
	Mean	*29.8*	*1.03*	*7.05*	*1.97*
	SD	*3.94*	*0.747*	*0.209*	*0.424*
	%RSD	*13.2*	*72.3*	*3.0*	*21.5*
2	1	22.0	3.17	15.6	4.57
	2	21.7	3.13	16.7	5.45
	3	18.4	2.76	15.1	5.14
	Mean	*20.7*	*3.02*	*15.8*	*5.05*
	SD	*1.61*	*0.184*	*0.674*	*0.365*
	%RSD	*7.8*	*6.1*	*4.3*	*7.2*
5	1	36.9	6.69	33.8	15.3
	2	44.2	6.79	32.6	17.0
	3	34.1	6.97	35.0	15.6
	Mean	*38.4*	*6.81*	*33.8*	*16.0*
	SD	*4.27*	*0.115*	*0.959*	*0.741*
	%RSD	*11.1*	*1.7*	*2.8*	*4.6*

* See Section 2.3.1 for subtraction of chloroform interference.

The range of the method across the related compounds is 0.2 to 10 µg L^{-1} for BTEX and 2 to 100 µg L^{-1} for the THMs. Note that the upper limit of quantitation is not a limitation of the SIFT-MS technique itself (*c.f.* Ref. [23]), but was an arbitrary upper limit defined prior to this study, because improving the LLOQs is the primary focus rather than maximizing the linearity range.

3.4. Precision

Precision (repeatability) was investigated by analyzing standards prepared at three concentrations (six replicates each). The data are summarized in Tables 6 and 7 for BTEX and the THMs, respectively, while data for all quantitation ions are provided in Tables S5 and S6 of the Supplementary Materials. At all levels the results are well within acceptance criteria (i.e., within ± 20% RSD [6]), even though no internal standard (ISD) is necessary in SIFT-MS, for reasons described in detail elsewhere [7].

Table 6. Precision data for BTEX at solution concentrations of 1, 5, and 9 µg L^{-1}. Reported data, mean, and standard deviation (SD) are shown in ppbV (headspace), while RSD is shown as a percentage.

Solution Conc./µg L^{-1}	Replicate No./*Statistical Parameter*	Benzene	Toluene	Ethylbenzene *	Xylenes *
1	1	17.2	16.4	13.3	11.7
	2	15.8	15.3	13.3	12.5
	3	13.2	13.2	10.9	11.7
	4	14.9	15.1	13.1	11.8
	5	16.4	14.8	12.1	13.3
	6	15.4	15.5	11.2	12.4
	Mean	*15.5*	*15.0*	*12.3*	*12.2*
	SD	*1.25*	*0.964*	*0.980*	*0.579*
	%RSD	*8.1*	*6.4*	*8.0*	*4.7*
5	1	95.9	94.8	74.4	79.9
	2	98.8	100	80.7	77.3
	3	109	106	94.7	85.9
	4	97.8	104	77.0	82.3
	5	110	104	78.0	80.7
	6	102	108	81.3	77.8
	Mean	*102*	*103*	*81.0*	*80.6*
	SD	*5.36*	*4.48*	*6.56*	*2.91*
	%RSD	*5.2*	*4.3*	*8.1*	*3.6*
9	1	196	197	158	156
	2	196	192	160	158
	3	171	178	143	135
	4	201	199	157	157
	5	187	188	153	154
	6	209	205	162	165
	Mean	*193*	*194*	*155*	*154*
	SD	*12.0*	*8.63*	*6.25*	*9.20*
	%RSD	*6.2*	*4.5*	*4.0*	*6.0*

* See Section 2.3.1 for deconvolution of ethylbenzene and the xylenes using the $O_2^{+\bullet}$ product ions.

Table 7. Precision data for the THMs (mean across quantitation ions) at solution concentrations of 10, 50, and 90 µg L^{-1}. Reported data, mean, and standard deviation (SD) are shown in ppbV (headspace), while RSD is shown as a percentage.

Solution Conc./µg L^{-1}	Replicate No./*Statistical Parameters*	Bromodichloromethane *	Bromoform	Chloroform	Dibromochloromethane
10	1	131	13.8	91.4	38.3
	2	96.3	14.5	94.8	37.8
	3	108	12.5	85.4	34.8
	4	106	13.7	92.7	34.7
	5	107	13.5	89.3	37.7
	6	95.7	14.4	95.2	40.2
	Mean	*107.3*	*13.7*	*91.5*	*37.2*
	SD	*11.7*	*0.647*	*3.39*	*1.96*
	%RSD	*10.9*	*4.7*	*3.7*	*5.3*

Table 7. *Cont.*

Solution Conc./µg L^{-1}	Replicate No./*Statistical Parameters*	Bromodichloromethane *	Bromoform	Chloroform	Dibromochloromethane
50	1	575	90.4	708	230
	2	559	85.2	732	229
	3	666	105	737	280
	4	534	85.7	721	239
	5	721	88.4	740	254
	6	663	94.0	771	263
	Mean	*620*	*91.4*	*735*	*249*
	SD	*67.4*	*6.63*	*19.5*	*18.7*
	%RSD	*10.9*	*7.3*	*2.7*	*7.5*
90	1	868	162	1458	428
	2	1043	153	1373	434
	3	878	151	1108	382
	4	1030	154	1353	443
	5	820	155	1408	414
	6	1132	163	1478	477
	Mean	*962*	*157*	*1363*	*430*
	SD	*113*	*4.47*	*122*	*28.7*
	%RSD	*11.7*	*2.9*	*9.0*	*6.7*

* See Section 2.3.1 for subtraction of chloroform interference.

Evaluation of intermediate precision and reproducibility parameters were outside the scope of this study.

3.5. Accuracy and Recovery

Accuracy and recovery were evaluated on drinking water from the town supply in Girton, Cambridge, UK (see Section 2.1). The measured concentrations of target compounds in six replicate water samples (for THMs, averaged across quantitation ions) are shown in Table 8, while data for individual quantitation ions is summarized in Tables S7 and S8 of the Supplementary Materials for BTEX and the THMs, respectively. It is evident that the present method is performing very well for the BTEX compounds—apart from one replicate of benzene falling on the LLOQ, the results demonstrate the absence of these compounds in drinking water. In contrast, for the THMs the results suggest that bromodichloromethane, bromoform and dibromochloromethane are all present above the LOQ, but still in the single-digit microgram-per-liter range. Table S8 shows that this observation is consistent across both/all quantitation ions, so it does not arise from an interfered ion biasing the calculation of the mean value. This suggests that the target compounds are present, but confirmatory analysis lies outside the scope of this study.

Table 8. Measured concentrations (in µg L^{-1}) in drinking water (Cambridge, UK) samples for BTEX and THMs. The mean, standard deviation (SD), and RSD (%) are also shown.

Amount/ µg L^{-1}	Benzene	Toluene	Ethylbenzene *	Xylenes *	Bromodichloromethane **	Bromoform	Chloroform	Dibromochloromethane
Repl. 1	<LOQ	<LOQ	<LOQ	<LOQ	2.41	8.25	<LOQ	3.94
Repl. 2	0.20	<LOQ	<LOQ	<LOQ	2.39	9.45	<LOQ	4.78
Repl. 3	<LOQ	<LOQ	<LOQ	<LOQ	6.51	7.62	<LOQ	4.49
Repl. 4	<LOQ	<LOQ	<LOQ	<LOQ	2.43	9.14	<LOQ	4.26
Repl. 5	<LOQ	<LOQ	<LOQ	<LOQ	2.03	8.85	<LOQ	4.00
Repl. 6	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	8.74	<LOQ	3.78
Mean	*N/A*	*N/A*	*N/A*	*N/A*	*2.93*	*8.67*	*N/A*	*4.21*
SD	*N/A*	*N/A*	*N/A*	*N/A*	*1.66*	*0.83*	*N/A*	*0.42*
%RSD	*N/A*	*N/A*	*N/A*	*N/A*	*56.9*	*9.7*	*N/A*	*9.8*

* See Section 2.3.1 for deconvolution of ethylbenzene and the xylenes using the $O_2^{+\bullet}$ product ions. ** See Section 2.3.1 for subtraction of chloroform interference.

Tables 9 and 10 summarize the accuracy data obtained for three replicates each of three spike levels in drinking water (2.5, 5.0, and 7.5 µg L^{-1} for BTEX and 25, 50, and 75 µg L^{-1} for the THMs). Independent standards were used in the subsequent analysis.

After the spikes were measured, the mean drinking water concentration was subtracted from the total to enable determination of spike recovery. The accuracy data for individual replicates of BTEX largely meet acceptance criteria (±20% [1]), while the THMs meet it only at the highest spike level. Poor accuracy is observed occasionally for chloroform and bromodichloromethane and propagates from a low chloroform measurement due to the subtraction required to calculate to bromodichloromethane. The cause of the low chloroform readings requires further investigation but could be an artefact arising from taking two injections from the same vial (e.g., a septum leak could repressurize the vial with laboratory air and effectively dilute the injection made solely for chloroform). Mostly accuracy measurements have RSDs less than 10%, demonstrating acceptable repeatability.

Table 9. Accuracy data (μg L^{-1} in solution) for each of the triplicate measurements of 2.5, 5.0, and 7.5 μg L^{-1} BTEX spikes in drinking water (Cambridge, UK). The mean, standard deviation (SD), and RSD (in %) are also shown.

Solution Conc./μg L^{-1}	Replicate No./*Statistical Parameter*	Benzene	Toluene	Ethylbenzene *	Xylenes *
2.5	1	2.29	2.09	2.05	2.30
	2	2.15	1.92	2.03	2.02
	3	2.26	2.02	2.14	2.12
	Mean	*2.24*	*2.01*	*2.07*	*2.15*
	SD	*0.060*	*0.067*	*0.047*	*0.12*
	%RSD	*2.7*	*3.3*	*2.3*	*5.4*
5.0	1	4.81	4.83	4.37	5.18
	2	4.66	4.18	4.61	4.97
	3	4.20	3.72	4.01	3.95
	Mean	*4.56*	*4.24*	*4.33*	*4.70*
	SD	*0.26*	*0.45*	*0.25*	*0.54*
	%RSD	*5.7*	*10.7*	*5.7*	*11.5*
7.5	1	7.18	6.68	7.39	7.31
	2	6.83	6.48	6.49	7.10
	3	7.24	6.68	6.57	7.88
	Mean	*7.08*	*6.62*	*6.82*	*7.43*
	SD	*0.18*	*0.094*	*0.41*	*0.33*
	%RSD	*2.5*	*1.4*	*5.9*	*4.4*

* See Section 2.3.1 for deconvolution of ethylbenzene and the xylenes using the $O_2^{+\bullet}$ product ions.

Table 10. Accuracy data (μg L^{-1} in solution) for each of the triplicate measurements of 25, 50, and 75 μg L^{-1} THM spikes in drinking water (Cambridge, UK). The mean, standard deviation (SD), and RSD (in %) are also shown. Concentration measurements are averaged across quantitation ions.

Solution Conc./μg L^{-1}	Replicate No./*Statistical Parameter*	Bromodichloromethane *	Bromoform	Chloroform	Dibromochloromethane
25	1	29.3	37.5	23.5	32.2
	2	35.0	46.0	19.6	33.9
	3	30.4	33.9	21.1	29.9
	Mean	*31.6*	*39.1*	*21.4*	*32.0*
	SD	*2.56*	*5.33*	*1.61*	*1.67*
	%RSD	*8.3*	*13.5*	*7.6*	*5.2*
50	1	112.2 **	64.4	29.8 **	58.6
	2	59.2	62.0	45.6	53.6
	3	39.4	51.5	42.7	47.7
	Mean	*70.3*	*59.3*	*39.4*	*53.3*
	SD	*30.7*	*5.69*	*6.86*	*4.56*
	%RSD	*43.7*	*9.6*	*17.4*	*8.6*

Table 10. *Cont.*

Solution Conc./μg L^{-1}	Replicate No./*Statistical Parameter*	Bromodichloromethane *	Bromoform	Chloroform	Dibromochloromethane
75	1	89.9	87.5	69.9	79.8
	2	83.7	77.8	65.9	72.6
	3	86.4	77.0	70.4	79.8
	Mean	*86.7*	*80.8*	*68.8*	*77.4*
	SD	*4.11*	*4.90*	*2.23*	*4.76*
	%RSD	*4.7*	*6.0*	*3.3*	*6.1*

* See Section 2.3.1 for subtraction of chloroform interference. ** As discussed in the text, chloroform measured low using its unique OH^- product ions and this impacts bromodichloromethane through subtraction of chloroform.

Recovery data obtained for triplicate measurements at the above levels in solution are summarized in Tables 11 and 12 for BTEX and the THMs, respectively. In line with the accuracy data, recoveries are largely acceptable (±20%) for BTEX, while at the two lower spike levels a significant number of values are not acceptable for the THMs. These observations are paralleled in the data obtained for the individual quantitation ions (see Supplementary Materials Tables S9 and S11 for the BTEX accuracy and recovery data, and Tables S10 and S12 for the THMs).

Table 11. Recovery data (%) for each of the triplicate measurements of 2.5, 5.0, and 7.5 μg L^{-1} BTEX spikes in drinking water (Cambridge, UK). Mean recovery, standard deviation (SD), and RSD are also shown.

Solution Conc./μg L^{-1}	Replicate No./*Statistical Parameter*	Benzene	Toluene	Ethylbenzene *	Xylenes *
2.5	1	91.8	83.5	81.8	92.0
	2	86.2	77.0	81.2	80.7
	3	90.4	80.9	85.5	84.9
	Mean	*89.5*	*80.5*	*82.8*	*85.9*
	SD	*2.4*	*2.7*	*1.9*	*4.6*
	%RSD	*2.7*	*3.3*	*2.3*	*5.4*
5.0	1	96.2	96.6	87.4	103.7
	2	93.3	83.5	92.2	99.4
	3	84.1	74.4	80.2	79.0
	Mean	*91.2*	*84.8*	*86.6*	*94.0*
	SD	*5.2*	*9.1*	*5.0*	*10.8*
	%RSD	*5.7*	*10.7*	*5.7*	*11.5*
7.5	1	95.7	89.1	98.5	97.4
	2	91.0	86.5	86.6	94.7
	3	96.5	89.1	87.6	105.0
	Mean	*94.4*	*88.2*	*90.9*	*99.1*
	SD	*2.4*	*1.3*	*5.4*	*4.4*
	%RSD	*2.5*	*1.4*	*5.9*	*4.4*

* See Section 2.3.1 for deconvolution of ethylbenzene and the xylenes using the $O_2^{+\bullet}$ product ions.

Table 12. Recovery data (%) for each of the triplicate measurements of 25, 50, and 75 μg L^{-1} THMs spikes in drinking water (Cambridge, UK) averaged across quantitation ions. Mean recovery, standard deviation (SD), and RSD are also shown.

Solution Conc./μg L^{-1}	Replicate No./*Statistical Parameter*	Bromodichloromethane *	Bromoform	Chloroform	Dibromochloromethane
25	1	105.7	115.2	92.8	112.1
	2	128.3	149.2	77.0	118.8
	3	109.9	100.9	83.3	102.9
	Mean	*114.6*	*121.8*	*84.4*	*111.3*
	SD	*9.8*	*20.2*	*6.5*	*6.5*
	%RSD	*8.6*	*16.6*	*7.7*	*5.8*

Table 12. *Cont.*

Solution Conc./μg L^{-1}	Replicate No./*Statistical Parameter*	Bromodichloromethane *	Bromoform	Chloroform	Dibromochloromethane
50	1	218.4 **	111.4	59.0 **	108.7
	2	112.6	106.7	90.5	98.7
	3	73.0	85.6	84.8	87.0
	Mean	*134.7*	*101.2*	*78.1*	*98.1*
	SD	*61.4*	*11.2*	*13.7*	*8.9*
	%RSD	*45.6*	*11.1*	*17.6*	*9.0*
75	1	116.0	105.1	92.8	100.7
	2	107.6	92.2	87.5	91.2
	3	111.3	91.1	93.5	100.8
	Mean	*111.7*	*96.1*	*91.3*	*97.6*
	SD	*3.4*	*6.3*	*2.7*	*4.5*
	%RSD	*3.1*	*6.6*	*2.9*	*4.6*

* See Section 2.3.1 for subtraction of chloroform interference. ** As discussed in the text, chloroform measured low using its unique OH^- product ions and this impacts bromodichloromethane through subtraction of chloroform.

3.6. Robustness

Evaluation of the analytical robustness was outside the scope of this preliminary study. No significant change is anticipated compared to results obtained in the previous study [18].

4. Discussion

In this section, the headspace-SIFT-MS results summarized above will be discussed in the contexts of (i) the limited prior research targeting these compounds in water using headspace-SIFT-MS, (ii) various regulatory limits (Table 1) and the United States regulatory PT-GC/MS method used to assess samples against US EPA limits, (iii) an alternative headspace-GC-μECD procedure, and (iv) alternative approaches using real-time MS and ion-mobility spectrometry. This broad survey enables some conclusions to be made on the suitability of SIFT-MS for analysis of BTEX and THMs in water in several areas of application.

Compared to previous work using headspace-SIFT-MS for water analysis [17,18], the results presented here represent a significant advance in LLOQs. Lee et al. [17] demonstrated a novel real-time monitoring approach built on a commercial headspace automation platform for analysis of wastewater contaminants. Their LLOQs are probably significantly compromised by the use of a transfer line between the autosampler and SIFT-MS inlet. Perkins and Langford [18] utilized a commercial inlet that is described elsewhere [15] and enables headspace to be injected without the use of a transfer line, significantly improving the LLOQs. In this work, the same inlet was used, but further improvement of LLOQs was achieved by increasing the incubation temperature, injection speed, and reducing the number of target compounds so that ion dwell times could be increased.

The LLOQs of 0.1 to 0.2 μg L^{-1} obtained for the BTEX compounds easily meet the EU [2], United States [1], and State of Florida [19] requirements where these exist (Table 1). For the THMs (SIFT-MS LOQs of 1 to 2 μg L^{-1}), comparison is less straightforward because no formal MCLs for the individual compounds are cited in the EU or US regulations. The US State of Florida has limits in place ([19]; Table 1), with the revised limits more favorable to headspace-SIFT-MS than earlier limits cited in a 2010 conference paper (0.21–5.67 μg L^{-1}) [34]. However, the revised limits for bromodichloromethane and dibromochloromethane lie very close to the method LLOQ of SIFT-MS. In contrast, the standard method utilized in the United States is US EPA Method 524.4 [6], which applies PT-GC/MS to provide lowest concentration minimum reporting levels (LCMRLs) that are significantly lower than HS-SIFT-MS (Table 13). Although headspace-SIFT-MS does not provide an alternative procedure to Method 524.4, the data presented demonstrate the potential for automated SIFT-MS to achieve very low detection limits for selected compounds in water with a throughput at least four times higher than PT-GC/MS.

Table 13. Headspace-SIFT-MS LOQs contrasted with a PT-GC/MS method (US EPA Method 524.4 [6]) and HS-GC-μECD [13]. All concentrations are μg L^{-1}.

Name	**PT-GC/MS [6] ***	**HS-GC-μECD [13]**	**HS-SIFT-MS [17]**	**HS-SIFT-MS [18]**	**HS-SIFT-MS (This Study)**
Benzene	0.022		119	1.14	0.10
Ethylbenzene	0.013			1.15	0.20
Toluene	0.034		133	1.15	0.10
Xylenes	0.17, 0.037 **			1.16	0.10
Bromodichloromethane	0.027	0.32			1.0
Bromoform	0.021	0.47	110		2.0
Chloroform	0.032	0.47		3.36	1.0
Dibromochloromethane	0.016	0.35			2.0

* Lowest concentration minimum reporting levels (LCMRLs) in US EPA Method 524.4 [6]. ** *m*- and *p*-xylene are 0.17; *o*-xylene is 0.037.

Recently Alexandrou et al. [13] developed a headspace-GC method using micro electron capture detection (GC-μECD) for THM analysis, which both simplifies sample preparation (1 min/sample) and shortens GC run time (10 min vs. 18 min for PT-GC/MS). Although the LLOQs are about an order of magnitude higher than PT-GC/MS, they still surpass those of headspace-SIFT-MS (Table 13) and easily meet the current requirements of the EU, US, and State of Florida regulations (Table 1). Headspace-SIFT-MS is currently disadvantaged compared to headspace-GC because it uses commercially available headspace systems designed for GC. These systems use headspace syringe volumes of relatively small volume that are designed for rapid injection of headspace into the GC inlet, whereas for SIFT-MS slow sample injection is necessary [7]. Headspace-SIFT-MS requires a make-up (dilution) flow to maintain a consistent ca. 25 mL min^{-1} flow at the sample inlet [15], which can be viewed as a mandatory split. This work has reduced the dilution level to five-fold—a value for which current syringe-injection autosampler technology does not enable improvement near-term. Future autosampler development should consider larger syringe volumes and would hence increase headspace-SIFT-MS sensitivities at least five-fold. Nevertheless, headspace-SIFT-MS has a sample throughput at least three times higher than headspace-GC-μECD with existing automation technology.

Regulatory laboratory-based analysis of THMs does not currently appear feasible for headspace-SIFT-MS, but can the improved performance demonstrated in this work be extrapolated to real-time process monitoring applications of the type explored in Korea [17] or to more continuous analysis [10–12]? Adoption of the improved sample delivery approach and analytical method described here should mean that drinking water MCLs are achievable on an automated sampling system, in addition to the higher Korean wastewater limits described in the earlier work [17]. Chloroform and dibromochloromethane should be readily measurable below the MCLGs (Table 1), but bromodichloromethane and bromoform will only report at the MCLGs and above.

Continuous measurement of VOCs from water has been demonstrated using membrane introduction-PTR-MS [10], spray inlet-PTR-MS [11,12], and membrane inlet-ion mobility spectrometry (MI-IMS) [35]. For MI-IMS, the LOD of 1 μg L^{-1} for benzene (using the more sensitive radioactive ion source) means that the technique is unsuitable for drinking water analysis because quantitation cannot be achieved at the EU MCL. The membrane introduction-PTR-MS study [10] investigated only oxygenated VOCs, but response times were slow due to migration through the membrane. The spray inlet-PTR-MS studies investigated benzene [11] and toluene [12], achieving LODs of 0.14 and 0.9 μg L^{-1}, respectively, which equate approximately to LOQs of 0.4 and 2.5 μg L^{-1}. These results compare favorably with the headspace-SIFT-MS BTEX data presented here, so the continuous monitoring application has merit for future research. However, it should be noted that neither membrane-introduction nor spray-inlet methods of sample introduction are truly real-time.

In summary, improved LOQs for headspace-SIFT-MS analysis of BTEX, bromoform, and chloroform have been demonstrated compared to previous studies [17,18]. In clean matrices, such as drinking water, SIFT-MS readily speciates ethylbenzene from the xylenes, and all THMs (by using a subtraction approach). LOQs of the THMs are approximately one order of magnitude higher than BTEX, due to the impact of headspace partitioning, volatility, and density in varying degrees. Improving the sample inlet on automated SIFT-MS inlets so that it can be heated above 150 °C may enhance LOQs for the brominated THMs, while development of larger headspace syringes for commercial autosamplers would provide an instant improvement in LOQs. As they stand, the SIFT-MS LOQs meet current regulatory requirements in the EU, US, and the state of Florida, but fall short of the LOQs achieved by PT- and headspace-GC methods developed for routine laboratory analysis. Nevertheless, headspace-SIFT-MS provides three-to-four-fold higher throughputs than the GC methods, which facilitates more rapid and economical screening opportunities. (For example, it could be applied to benzene, which recently has become of significant concern in some personal care products [36].) In addition to laboratory-based analysis, a major advantage of DIMS methods over GC is the ability to analyze in real time; the results obtained here look promising for extending field-based real-time analysis of VOCs from wastewater [17] to drinking water. This is an area for potential future research, which should also cover a broader range of drinking water samples, preferably measured in parallel with GC.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/environments9100124/s1, Figure S1: Linearity of the BTEX compounds; Figure S2: Linearity of individual quantitation ions of the THM compounds; Table S1: Linearity data for the BTEX compounds; Table S2: Linearity data for the individual quantitation ions of the THM compounds; Table S3: Limit of quantitation data for the BTEX compounds; Table S4: Limit of quantitation data for the individual quantitation ions of the THMs; Table S5: Precision data for the BTEX compounds; Table S6: Precision data for the individual quantitation ions of the THMs; Table S7: Measured BTEX concentrations in a drinking water sample; Table S8: Measured THM concentrations (individual quantitation ions) in a drinking water sample; Table S9: Accuracy data for BTEX compounds; Table S10: Accuracy data for the individual quantitation ions of the THMs; Table S11: Recovery data for BTEX compounds; Table S12: Recovery data for the individual quantitation ions of the THMs.

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Conflicts of Interest: M.P. is an employee of Element Materials Technology Laboratory Instrumentation in Cambridge, United Kingdom (formerly Anatune), a distributor of commercial SIFT-MS instruments in the United Kingdom and the Republic of Ireland. V.L. is an employee of Syft Technologies Limited, a manufacturer of commercial SIFT-MS instruments.

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